LETTER to the EDITOR

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Letter to the Editor: Reference standards and the interpretation of diagnostic accuracy in visually directed hysteroscopic biopsy

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Dear Editor,

We read with great interest the Joint Society Practice Guideline from AAGL–ESGE–GCH on visually directed hysteroscopic biopsy for abnormal uterine bleeding (AUB) and postmenopausal bleeding (PMB).[1] We wish to highlight a methodological point relevant to interpreting its diagnostic accuracy estimates: the heterogeneity of reference standards across the four included comparative studies.

Of the four studies, three were judged to have a high overall risk of bias.[1] The reference standard also varied: Leone et al.[2] used blind dilatation and curettage (D&C); Gao et al.[3] and Karageyim Karsidag et al.[4] used hysteroscopically directed biopsy; and Angioni et al.[5] used different reference standards depending on pathology, including operative hysteroscopy, hysterectomy, and, after a negative hysteroscopy, an unspecified endometrial biopsy.[1] Because sensitivity and specificity are defined relative to the reference standard used, these differences limit direct comparison across studies. For malignancy, for example, sensitivity for hysteroscopy-directed biopsy was reported against blind D&C in one study and against a different reference standard in another,[1] so the two estimates cannot be read as measuring the same thing.

This does not weaken the clinical rationale for targeted sampling; rather, it means the comparative estimates should be interpreted alongside how each reference diagnosis was established. Comparative diagnostic accuracy studies are particularly sensitive to differences in patient selection, index-test conduct, reference-standard definition, and study flow domains assessed by the QUADAS-C tool.[4] When reference standards differ between studies, apparent differences in diagnostic performance may partly reflect differences in verification rather than genuine differences between the tests.

We suggest that future comparative studies of hysteroscopy versus blind sampling prespecify a clinically appropriate reference standard, apply it consistently across comparison groups, and clearly report when tissue from the index procedure itself contributes to the reference diagnosis. Distinguishing visual hysteroscopic impression from histopathological confirmation, especially when malignancy is suspected,

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would further strengthen future evidence syntheses and their translation into settings where hysteroscopy is not universally available.

We support the guideline's emphasis on visually directed sampling and believe a more consistent evidence base would further strengthen recommendations for evaluating AUB and PMB.

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